Claims

1. An isolated polynucleotide molecule comprising a mutant allele of thiopurine S-methyltransferase (TPMT) gene or fragments thereof containing single nucleotide polymorphisms (SNPs 1- 41) as shown in Table 1.

2. An isolated polynucleotide molecule comprising a mutant allele of thiopurine S-methyltransferase (TPMT) gene or a fragment thereof containing at least two or more of single nucleotide polymorphisms (SNPs 1- 41) as shown in Table 1.

3. An isolated polynucleotide molecule comprising a mutant allele of thiopurine S-methyltransferase (TPMT) gene or fragments thereof containing single nucleotide polymorphisms, SNPs 10 and/or 17, and/or 26 and 29 in the following haplotypes (combinations):

   a) SNP 26 being MT (GG) and SNP 29 being WT (GG)

   b) SNP 26 being HT (AG) and SNP 29 being WT (GG)

   c) SNP 26 being MT (GG) and SNP 29 being HT (AG)

   d) SNP 10 being MT (TT) and SNP 17 being MT (GG)

   e) SNP 10 being HT (AT) or MT (TT) and SNP 17 being WT (TT)

   f) SNP 10 being MT (TT) and SNP 17 being HT (GT)

   g) SNP 10 being HT (AT) or WT (AA) and SNP 17 being HT (GT)

   h) SNP 10 being WT (AA) and SNP 17 being MT (GG).

4. An isolated polynucleotide molecule comprising a mutant allele of thiopurine S-methyltransferase (TPMT) gene or fragments thereof containing single nucleotide polymerphisms, SNPs 7, 8, 20 and/or 26 and 27 in the following haplotypes (combinations):

   a) SNP 7 being MT (AA) and SNP 8 being WT (TT) and SNP 20 being MT (AA) and SNP 26 being WT (AA) and SNP 29 being WT (AA)

   b) SNP 7 being MT (AA) and SNP 8 being WT (TT) and SNP 20 being HT (AT)

   c) SNP 7 being WT (TT) and SNP 8 being HT (AT) or MT (AA) and SNP 20 being WT (TT).

5. An isolated polynucleotide molecule fully complementary to any one of the polynucleotide molecules of claims 1 - 4.

6. A diagnostic assay or kit for determining thiopurine S-methyl-transferase (TPMT) genotype of a subject which comprises

a) isolating nucleic acid from said subject;

b) amplifying specifically a thiopurine S-methyltransferase (TPMT) PCR fragment with primers of Table 2 from said nucleic acid, which includes at least one of SNPs of claims 1 - 4 thereby obtaining an amplified fragment; and

c) genotyping the amplified fragment obtained in step b), thereby determining the thiopurine S-methyltransferase (TPMT) genotype or haplotype of said subject,

d) the kit comprising sequence determination primers and sequence determination reagents, wherein said primers are selected from the group comprising primers that hybridize to polymorphic positions in the human TPMT genes according to claims 1 - 4; and primers that hybridize immediately adjacent to polymorphic positions in the human TPMT gene according to claims 1 - 4.

7. A kit as defined in claim 6 detecting a combination of two or more, up to all, polymorphic sites selected from the groups of sequences as defined in claim 1 - 4.

8. A method for determining a patient's individual response to thiopurine therapy, including drug efficacy and adverse drug reactions, comprising determining the identity of nucleotide variations according to claims 1 - 4.